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## Adverse childhood experiences and risk of type 2 diabetes: A systematic review and meta-analysis



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### ABSTRACT

**Aims.** It is evident that adverse childhood experiences (ACEs) can influence health status of adult life, but few large-scale studies have assessed the relation of ACEs with type 2 diabetes. This meta-analysis aimed to summarize existing evidence on the link between ACEs and type 2 diabetes in adults.

**Materials and method.** We searched all published studies from PubMed and EMBASE before Aug 2015 using keywords like adverse childhood experiences and diabetes, and scanned references of relevant original articles. We included studies that reported risk estimates for diabetes by ACEs and matched our inclusion criteria. We examined the overall relationship between ACEs and diabetes, and stratified the analyses by type of childhood adversities, study design and outcome measures, respectively.

**Results.** Seven articles fulfilled the inclusion criteria for this Meta-analysis, comprising 4 cohort and 3 cross-section studies. A total of 87,251 participants and 5879 incident cases of type 2 diabetes were reported in these studies. The exposure of ACEs was positively associated with the risk of diabetes with a combined odds ratio of 1.32 (95% confidence interval 1.16 to 1.51) in the total participants. The influence of neglect was most prominent (pooled odds ratio 1.92, 95% confidence interval 1.43 to 2.57) while the effect of physical abuse was least strong (pooled odds ratio 1.30, 95% confidence interval 1.19 to 1.42). The pooled odds ratio associated with sexual abuse was 1.39 with the 95% confidence intervals from 1.28 to 1.52.

**Conclusions.** The results support a significant association of adverse childhood experiences with an elevated risk of type 2 diabetes in adulthood.

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**Abbreviations:** ACEs, adverse childhood experiences; BMI, body mass index; PTSD, psychiatric disorders even posttraumatic stress disorders; DB, diabetes; OR, odds risks; CI, confidence interval; SES, socioeconomic status; SND, standard normal deviate.

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## 1. Introduction

Type 2 diabetes has become a severe public health problem in many parts of the world during recent decades. The mortality of this disease was doubled from 1990 and accounted for 1.3 million deaths globally in the year 2010 [1]. Being a typical chronic uncommunicable disease, type 2 diabetes also confers a major hazardous factor for stroke and ischemic heart disease — the latter two killed an estimated 12.9 million people worldwide in 2010 [1,2]. In the view of a previous report, genetic heredity and personal life style such as diet and smoking habits, played important roles in the development of type 2 diabetes [3]. At same time, a growing body of research has delved to search for contributing factors from early life such as childhood adversities.

Adverse childhood experiences (ACEs) include physical and sexual abuse, neglect, and many other types as defined in early studies [4–6]. ACEs are common in the population regardless of sex and cultural settings. It was reported that nearly 4%–16% of children were physically abused and 10% of them were neglected or psychologically abused each year in high-income countries, including USA, UK, New Zealand, and Finland [7]. For sexual abuse, 5% to 10% of girls and up to 5% of boys were exposed to penetrative sexual abuse during childhood, and three times this number were exposed to any type of sexual abuse in the developed countries including New Zealand, Australia, USA, and Canada [7,8]. The exposure rates could be higher if taking into account cases that were unable to be verified due to protective services as well as cases that were not reported or discovered [9]. According to a recent report from European Union, almost one in three European women had suffered violence or sexual abuse and one over ten women had experienced sexual violence before turning 15 years old [10]. Moreover, physical abuse was most common among various types of ACEs and presented in 18.6% of the study population from eight European countries [11]. There are relatively less comprehensive reports on these problems from Asia. But in China, for instance, a large amount of children in rural areas has to live apart from their parents who strive in big cities for job opportunities, being left behind and to a certain degree neglected by their parents [12,13].

It is well known that childhood experiences have profound influence on adult health [14]. They can not only affect one's psycho-social well-being [15,16], but also play an important role on one's physical condition in adulthood. A number of studies have shown that childhood adversities are associated with physical illnesses such as heart disease, stroke and chronic respiratory diseases, possibly through specific genes, induced inflammation or other mechanisms [17–20]. In search of evidence linking ACEs and type 2 diabetes, however, no study has provided sufficient evidence on this relationship, and the existing literature relies heavily on cross-sectional designs. In order to get an overview, we conducted the present review with a meta-analysis on all published studies [21–27] that focused on childhood adversities and incidence of type 2 diabetes in adulthood.

## 2. Materials and Methods

### 2.1. Search Strategy

We conducted a literature search, up to Aug 2015, of PubMed (Medline) and EMBASE for all published studies examining the association between childhood adverse experiences and risk of type 2 diabetes. The search terms were “diabetes” or “type 2 diabetes” or “diabetes mellitus” or “type 2 diabetes mellitus” and “adverse childhood experiences” or “childhood adversities” or “childhood abuse” or “childhood maltreatment” or “child trauma” or “adverse childhood events”. In addition, we supplemented this search with a manual search of references from selected articles.

The studies included in this meta-analysis should meet the following criteria: 1) the study design was prospective cohort, cross-sectional, or case-control design; 2) type 2 diabetes was the definite outcome; 3) the exposure of interest was childhood adversities including physical abuse, sexual abuse, neglect, etc.; 4) odds risks or relative risks with 95% confidence intervals were reported. Types of studies excluded from our analysis included animal studies, clinical trials, reviews, letters and studies without sufficient data. Additionally, we applied a criterion of study quality to evaluate all included studies.

### 2.2. Data Extraction

We used a standard extraction form to collect the following information from each study: first author, publication year, study location, study design, participants, characteristics, year of follow-up, ACEs exposures and assessment methods, outcome measures and assessment methods, sample size, key results (odds ratio and 95% confidence intervals), and covariates included for adjustment. We also applied the Newcastle–Ottawa quality assessment scale [28] to assess the quality of the included studies. This scale is widely used for assessment of the quality of nonrandomized studies [29,30], and provides a grade from zero to nine points referring to the lowest to the highest quality. The scale comprises four items assessing the quality of participant selection and exposure measurement, three assessing the measures of outcomes and adequacy of follow-up, and two assessing the comparability of cohorts on the basis of study design and data analysis.

Two investigators independently performed the search of literature and carried out data extraction. Discrepancies, if any, were resolved by discussion and consultation with a third reviewer.

### 2.3. Statistical Analysis

We chose to present odds ratios and 95% confidence intervals as the effect size for all studies because all included studies used odds ratios in their results except the study by Rich-Edwards et al. [22] which applied hazard ratio. For two studies [22,24] reporting the separate effect of specific types of childhood adversities, we treated them as different studies when examining each type of ACEs. Also, two of included

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